

Chronic Diseases in the Rubber Industry

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An overview is presented of epidemiologic studies of chronic diseases in the rubber industry. Analyses of the mortality experience during the period 1964-1972 of workers age 40-64 and retirees age 65-84 of two large rubber and tire manufacturing companies consistently disclosed excesses of deaths attributed to leukemia and lymphosarcoma, and for cancers of the stomach, large intestine, and prostate. The relation of site-specific malignancies to work histories and grouped occupational titles as surrogate measures of work-related exposures to possible carcinogens is described. There was no evidence of company-wide, sizable, consistent excess for the other major chronic diseases causes of death.

Although a total cohort deficit in the mortality rate for lung cancer was found, there was a history of increased frequency of exposure to certain work areas among lung cancer decedents.

Morbidity studies, including analysis of disability retirements, and ad hoc questionnaire and health testing surveys, disclosed excesses of chronic pulmonary diseases. There was evidence of an interactive effect in the association of work and smoking histories with pulmonary disability retirement.

Introduction

The determination of the burden of chronic diseases in any population is a challenging epidemiologic problem. Further, to assess the contribution of environmental exposures at the work site to the amount and types of chronic disease in a population greatly complicates the analytic problem. The chronic diseases in an industrial society represent a large, diverse collection of disorders, each of which has its own set of etiologic factors. Most are of unknown etiology, but as our knowledge accumulates it would appear that the majority of, if not all, chronic diseases are the result of multiple causes. While not denying the importance of isolated instances in which occupational exposure to single agents produces specific diseases, it is more likely that understanding and eventual control of most chronic diseases will be achieved by studying the joint effects of exposures to multiple physicochemical agents, in

some cases, in relation to the personal and social characteristics of workers.

We shall present an overview of some of the research performed by the Occupational Health Studies Group of the University of North Carolina. These studies were designed in response to the expressed needs of the joint occupational health committees of the United Rubber Workers Union and the major rubber and tire manufacturing companies in the United States to identify hazards in the work environment and assess the health of the rubber workers covered by contract.

The identification of the need for this research followed the pioneering studies of Mancuso (1) in this country and subsequently the British rubber workers' experience as reported from morbidity studies by Parkes (2) and mortality studies by Fox et al. (3).

We organized our research in a multidisciplinary mode with equal representation of environmental sciences, biostatistics, and epidemiology in all major studies. Where indicated, a large number of other disciplines, including toxicology, genetics, computer sciences, and medical sociology, have been involved. In the

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results presented today, however, the focus will be on epidemiologic investigations.

In these epidemiologic investigations, we have measured the occurrence and sequelae of chronic disease among rubber workers, as manifested along a spectrum extending from expressed symptoms and discomfort, through absenteeism and work disability, to premature death. Two types of objectives underlie each of our investigations. One is to contrast the magnitude of these disorders in the contract-covered rubber workers with otherwise comparable workers in other industries. The second objective is to identify the existence, if any, of high risk subgroups within our studied populations, characterized by their patterns of work history and personal attributes.

We first present an overview of general studies of mortality for causes of death attributed to the major categories of chronic diseases, more specifically malignant neoplasms, cardiovascular diseases, diabetes, and chronic respiratory disease.

Mortality Studies

The derivation and analysis of company or industry-wide mortality rates offers a surrogate measure, as an approximation to the incidence of chronic diseases in rubber workers. The limitations of information of this type are many and well known, but for the purposes at hand, are of two major types. Firstly, mortality rates reflect but the attributed underlying cause of death and for many of the chronic diseases are not representative of the prevalence of the disorders at time of death. Additionally, mor-

tality rates are a composite of both incidence and case-fatality rates and there is no necessary relationship between environmental exposures at time of onset of the disease and either the progression of the disease or its final termination. In addition to these general limitations in the use of mortality rates, there is the specific limitation in this instance of presenting pooled, company-wide data across multiple plants, departments, processes and environmental exposures. Information of this type can be regarded at best as first level screening. Mortality excesses, if found, may reflect personal rather than occupational characteristics. They are, however, important in pointing to a disease excess in the aggregate of rubber workers and providing priorities for more specific research; failure to detect aggregated mortality excesses provides no assurance that high risks are not present within subgroups of workers with different exposures.

Table 1 presents a composite of data previously published separately by Andjelkovic et al. (4) and McMichael et al. (5) and represents the experience of two large cohorts using the same criteria of eligibility; namely subjects achieving age 40, with 10 or more years of prior service and vested pension rights with the company; the same period of observation and follow-up (1964–1972) with the same high rate of completeness of ascertainment of deaths; and with cause of death commonly coded by the same nosologist using the Eighth Revision of the International Classification of Diseases. A modified life table analysis was employed for the period of follow-up, and standardized mortality ratios (SMRs) were com-

Table 1. Mortality ratios in two cohorts of male rubber workers, Akron 1964–1972: age–sex standardized mortality ratios for major causes of death.

	Age groups 40–64		Age groups 65–84	
	Company A	Company B	Company A	Company B
Number of men	4576	6058	2102	2880
Causes of death with moderate and consistent excesses				
Malignant neoplasm				
Leukemia	315	100	128	139
Lymphosarcoma	251	147	226	108
Stomach	219	114	187	111
Prostate	147	183	142	110
Large intestine	121	102	123	113
Diabetes	157	137	143	120
All causes	93	89	99	93

puted by the indirect method, using the age-specific death rates of the U.S. male population of 1968 as the standard.

The SMRs are presented separately for men aged 40-64 and aged 65-84 for each company. Causes of death are grouped by whether or not there are consistent excesses of mortality rates.

It will be noted that there are consistent excesses within the four age-company subgroups studied for several malignant neoplasms; most conspicuously for leukemia and lymphosarcoma, and for cancer of the stomach, large intestine, and prostate. The SMRs were all higher than for all causes combined and ranged from 100 to 315. Mortality ratios for the total of all malignant neoplasms were slightly but statistically significantly higher than for all causes (Table 2). One major nonmalignant disease was noted with excess in the SMR for both companies in each of the age groups studied, namely diabetes, with SMRs ranging from 120 to 157.

Causes of death with slight but consistent excess mortality are grouped in Table 2. Within the cardiovascular diseases specifically identified, ischemic heart disease and cerebrovascular disease, in seven of the eight comparisons within companies and age bands, the SMRs for the specific disorders were equal to or greater than the SMR for all causes. However, in no instance was the SMR markedly elevated, the largest value being an SMR of 113 for cerebrovascular disease among 40-64 year-old males in Company B. In contrast, there was a consistent and significant deficit of cancer of the respiratory system and no evidence of consis-

tent excess for other malignancies such as cancer of the bladder. Similarly, there was no evidence of consistent excess for deaths attributed to chronic respiratory disease. We shall return to a consideration of these findings later.

Thus, on overview, deaths attributed to several site-specific malignancies and deaths attributed to diabetes were present with consistent and moderate excess. For the other major causes of death, there was no evidence of major, consistent excess.

The interpretation of standardized mortality ratios of this type must be tempered by their noncomparability across companies if different weights are used in each standardization. In fact, the age distributions of these two companies were quite similar. The important finding is the similarity of excesses for specific causes in comparison with all causes of mortality within age and company groups. We also believe that the identification of mortality excesses is a conservative one, particularly for the nonmalignancy causes, due to the healthy worker effect which we have investigated for these populations and reported elsewhere (6, 7). While it is customary to regard an SMR of 100 as expected and thus anything higher as evidence of excess mortality, the selection process associated with working, referred to as "the healthy worker effect," would indicate that in the absence of any industrial health hazard the SMRs of workers compared to the general population might be in the range of 60-80.

Detailed study of the work histories of decedents in comparison with control groups have begun to identify the characteristic work his-

Table 2. Mortality ratios in two cohorts of male rubber workers, Akron 1964-1972: age-sex standardized mortality ratios for major causes of death.

	Age groups 40-64		Age groups 65-84	
	Company A	Company B	Company A	Company B
Number of men	4576	6058	2102	2880
Causes of death with slight and consistent excesses				
Cardiovascular				
Ischemic heart disease	103	96	99	95
Cerebrovascular disease	85	113	103	98
All malignant neoplasms	100	93	103	96
Causes of death without consistent excesses				
Cancer of bladder	80	81	73	113
Cancer of respiratory system	72	83	84	79
Chronic respiratory disease	96	77	96	92
All causes	93	89	99	93

tories and possible exposures for the malignancies which appear in excess.

We have approached this problem by developing a computerized system to group each of the hundreds of job titles by groupings related to production processes (8). One grouping to test the association of leukemia deaths with solvent exposure is presented in Figure 1.

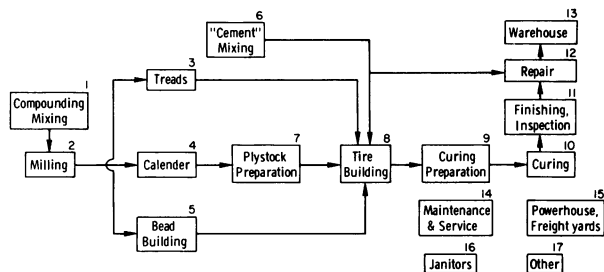


FIGURE 1. Diagrammatic representation of rubber tire production stages.

Stages 3, 4, and 6, respectively are treads, calendar, and cement mixing production stages with potential for high solvent exposure. Stages 13 and 15, for example, contain no solvent exposure jobs. Each of many occupational titles were suggested by potential for solvent exposure.

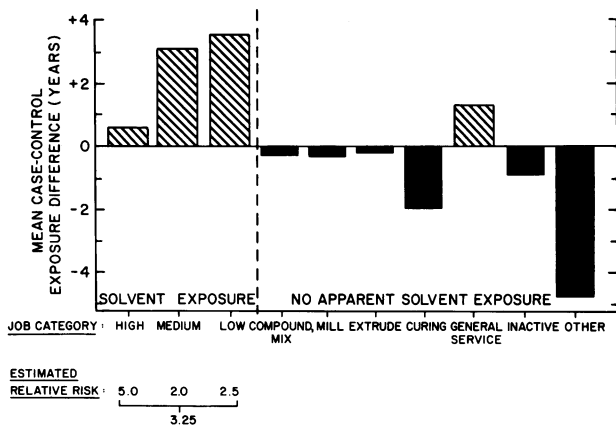


FIGURE 2. Mean differences in duration of exposure to job categories between 17 lymphatic leukemia cases and 51 individually matched controls, by level of solvent exposure. Note: The estimated relative risk of lymphatic leukemia for solvent-exposed workers was calculated by using the "discordant matched sets" formula.

The results of a case control study of the work history of leukemia decedents are presented in Figure 2; there is a marked contrast in work history with potential for solvent exposure in cases of leukemia in comparison with controls. Cases were more likely than controls to have work histories of jobs with solvent exposure potential. The estimated relative risk of leukemia deaths for workers with a history of exposure was 3.25.

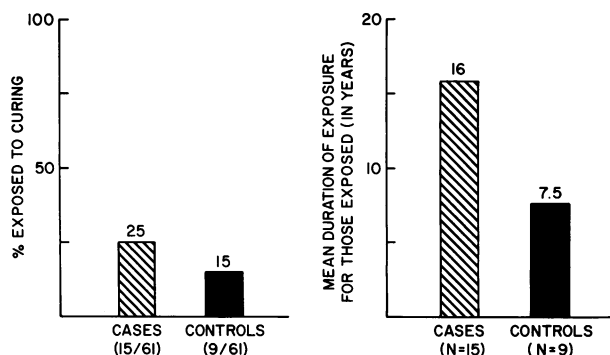


FIGURE 3. Exposure to curing process in 61 cases of lung cancer and 61 matched controls.

Equally important as the study of work histories for leukemia and lymphomas, which are causes of death appearing in excess, analysis of occupation titles and potential exposures has demonstrated an increased frequency of exposure to certain work areas among decedents (in three selected plants) with cancer of the respiratory system, despite the previous findings of a general total company deficit in the mortality rate for this same attributed cause of death.

Figure 3 demonstrates that lung cancer cases were more likely to have had a history of working in curing, 25% ($\pm 5.5\%$) of cases contrasted with 15% ($\pm 4.5\%$) of controls, and of those with a history of working in curing, cases had a longer duration than controls, 16 years compared with 7.5. The overall deficit is due to the small percentage working in exposed areas and illustrates how aggregated data of a total plant, across many work areas, may mask important exposure risk, within specific working groups.

A detailed systematic investigation of the work histories of decedents with many specific causes of death is underway. The data for one

Table 3. Age-standardized risk ratios (relative risk) for death, 1964-1973, from selected causes, among workers with at least 5 yr exposure to a specific work area, during 1940-1960, relative to all other workers.

Cause of death	Occupational title group	Risk ratio	
		Point estimate	99.9% Confidence interval
Stomach cancer	Compounding, mixing; cement mixing	2.0	1.6-2.9
	Mill-mixing	2.0	1.3-4.0
	Extrusion, tread cementing	2.3	1.7-3.6
	Synthetic plant	2.2	1.4-4.3
Colorectal cancer	Extrusion, tread cementing	2.2	1.6-3.4
	Maintenance	1.8	1.4-2.5
Respiratory cancer	Receiving and shipping	1.9	1.4-2.9
	Compounding, mixing; cement mixing	1.4	1.1-2.0
	Mill-mixing	2.1	1.4-4.3
	Extrusion, tread cementing	1.4	1.0-2.1
	Reclaim	2.3	1.6-3.9
Prostate cancer	Compounding, mixing; cement mixing	1.6	1.2-2.3
	Calendering	2.4	1.9-3.3
	Janitorial, trucking, etc.	3.5	2.8-4.6
Bladder cancer	Compounding, mixing; cement mixing	1.3	0.8-3.8
	Milling	2.4	1.6-4.0
	Reclaim	2.5	1.8-4.1

company (9) in Table 3 are presented for illustrative, overview purposes only, not for the detailed study of its content. It is intended in this context to illustrate the results of the approach taken, the numerous comparisons and the resulting methodologic problems. For example, recognizing the potential for chance findings, given multiple comparisons, we have set confidence intervals at 99.9%. Statistically significant differences in occupational title work histories are demonstrated for each listed cause of death. However, before attributing any of these causes of death to specific occupational exposures, we are replicating the studies to rule out personal characteristics (such as smoking or ethnicity, for example) as possible confounding factors responsible for the associations found with work histories. This highlights an important opportunity in our ability to replicate our studies in plants making similar products.

Morbidity Studies

Recognizing the limitations in mortality analyses to identify some chronic diseases, more particularly to identify any occupational determinants of these chronic diseases, we have been experimenting with alternate modes of screening large populations of rubber workers and

have been testing the utility of questionnaires and secondary analysis of such sources of morbidity data as sickness absenteeism, hospitalization and disability retirement records. The results which are to be presented are a small sample of a large number of surveys performed in different plants of different companies, in different parts of the country, and are neither necessarily representative of the entire industry, nor necessarily directly comparable one set of results to the other.

One approach to determining the relationship of chronic respiratory disease to the work environment was undertaken in one plant, ascertaining pulmonary disability retirements and carrying out a detailed case control study of the work history of these individuals. In this work of Lednar et al. (10), each pulmonary disability retiree was compared with two age/sex matched controls, who were non-disabled, and another set of two age/sex matched controls, who were disabled for causes other than pulmonary disease (Table 4). The most frequently attributed cause of pulmonary disability retirement was chronic obstructive pulmonary disease, accounting for 64% of all the pulmonary disability retirements; and emphysema alone with the attributed cause in 53% of all cases. A comparison of the work history characteristics of cases and controls showed that

Table 4. Occupational determinants of chronic disabling pulmonary disease in rubber workers in selected work areas.

Occupational exposure	Duration of service, yr/100 persons at risk		
	Pulmonary disability retirees (N=73)	Disabled controls (N=146)	Nondisabled controls (N=146)
Contact, dust	22.4	19.4	22.2
Talc	20.2	22.8	26.1
Carbon black	7.6	10.0	12.4
Contact, fumes	18.7	18.6	20.6
Work areas			
Mixing	5.6	4.6	15.2
Tirebuilding	17.2	14.8	15.2
Curing preparation	37.2	1.1 ^a	0.8 ^a
Curing	9.1	6.3 ^b	4.5 ^b
Finishing and inspection	7.7	3.8 ^b	4.6

^a $p < 0.01$.

^b $p < 0.05$.

cases were older at employment, started their careers in the rubber industry at a later point in historical time, and as a consequence had shorter total service durations in the rubber industry.

Table 4 displays the durations of service for cases and controls in selected occupational exposure areas. Because of group differences in total employment duration, comparisons are expressed in terms of person years at risk. From this table, it is apparent that cases have spent slightly more time in generally dusty

areas than disabled controls, but durations were similar to those of non-disabled controls. Cases spent less time in areas specifically involving exposure to talc and carbon black. This raises the possibility of selective occupational mobility out of irritating environments, by symptomatic workers. In contrast, the cases have spent significantly greater lengths of time in the areas involving curing preparation, curing and finishing and inspection.

In view of the overriding importance of cigarette smoking in association with chronic pul-

Table 5. Occupational determinants of chronic disabling pulmonary disease in rubber workers: relative risk of pulmonary disability retirement associated with occupational exposure and smoking among cases (N=48) and nondisabled controls (N=112).

Occupational exposure	Relative risk ^a		
	- Working + Smoking	+ Working - Smoking	+ Working + Smoking
Contact, dust	3.30	3.16	9.54 ^b
Talc	2.31	1.38	4.05 ^b
Carbon black	3.48 ^b	6.75	3.97 ^b
Contact, fumes	4.14	4.20	6.91 ^b
Work area			
Mixing	3.09 ^b	3.38	8.68 ^c
Tirebuilding	1.86	0.49	3.74 ^b
Curing preparation	3.19	7.25	16.31 ^c
Curing	2.36	1.71	7.38 ^c
Finishing and inspection	2.46	2.08	7.69 ^c

^a Relative to nonexposed, nonsmokers = 1.00.

^b $p < 0.05$.

^c $p < 0.01$.

monary disease, the odds ratio, or estimated relative risk, of pulmonary disability retirement was calculated for cases contrasted with controls, in relationship to occupational exposure and smoking history. As set out in Table 5, significant associations were demonstrated for contact with dust, fumes and selected work areas, particularly the curing preparation area. In each specific work area, there was evidence of an interactive effect in the association of work and smoking histories with pulmonary disability retirement.

For each work area identified, the risk of pulmonary disability retirement was significantly higher when the retiree had a history of smoking. For example, the estimated risk ratio of pulmonary disability for smokers without a history of working in the curing area was 2.4; for nonsmokers with a history of working in the curing area, it was 1.7; however for workers with a history both of smoking and curing area work, the estimated risk of pulmonary disability retirement was 7.4 times that for nonsmokers without curing area work history.

The identification of work areas with increased risk of pulmonary disability assumes added importance when it is recalled that in the mortality analyses of chronic respiratory disease, the SMR for the aggregate for all workers was not elevated.

We next set out to compare the reported prevalence of respiratory symptoms based on responses to the MRC questionnaire in a sample of rubber workers in one plant with those in other industries. As set out in Figure 4, there is a markedly higher prevalence of phlegm, persistent cough and phlegm, and of chest illness among these rubber workers than among samples of postal and transit workers (11) and telephone men (12). We emphasize once more the preliminary nature of these data, and the ecologic nature of their aggregated presentation. We do point out, however, that the higher prevalence of major respiratory symptoms is present in a population of rubber workers with validation of the questionnaire by ventilatory capacity measurements. Additionally, although there is a strong association of smoking with symptoms, the history of cigarette smoking was markedly lower in these rubber workers, than the other comparison groups. Detailed inquiry is now underway in a much larger sample of workers at two plants, relating workers' respiratory symptoms to their indi-

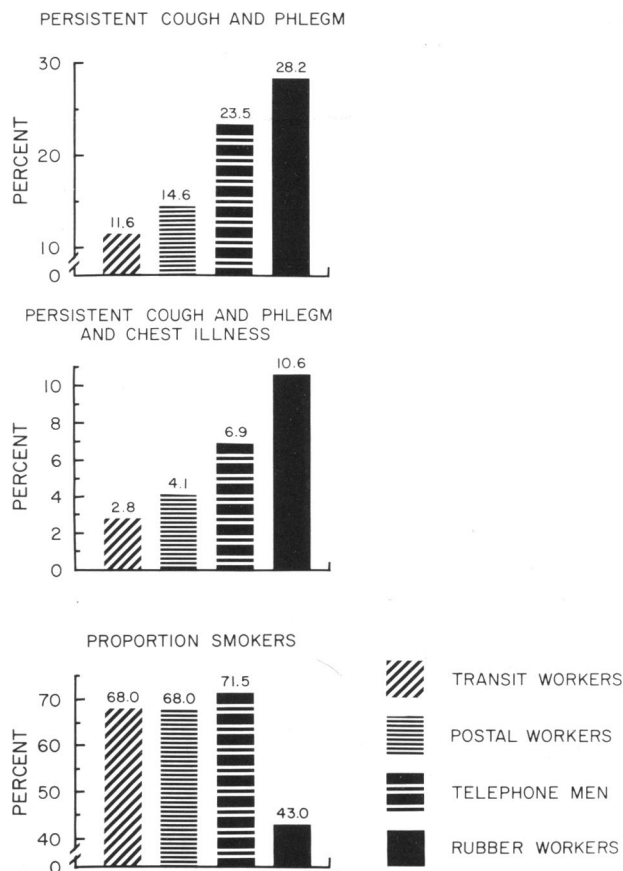


FIGURE 4. Prevalence of respiratory symptoms in white males of U.S. industrial populations: percentage of positive findings.

vidual occupational histories, both current and cumulative.

In summary, then, the determination of the burden of chronic diseases in any population is a challenging epidemiologic problem. Further, to assess the contribution of environmental exposures at the work site to the amount and types of chronic disease in a population greatly complicates the analytic problem. The chronic diseases in an industrial society represent a large, diverse collection of disorders, each of which has its own set of etiologic factors. Most are of unknown etiology, but as our knowledge accumulates it would appear that the majority of, if not all, chronic diseases are the result of multiple causes. While not denying the importance of isolated instances in which occupational exposure to single agents produces specific diseases will be achieved by studying the

joint effects of exposures to multiple physicochemical agents, in some cases, in relation to the personal and social characteristics of workers.

It was clear when we initiated our efforts that attention would have to be focused on the risk of malignancies secondary to chemical carcinogens. We think that the epidemiologic evidence now is convincing that there are instances of moderate excesses of selected malignancies, in relation to work histories in rubber workers, excesses which in some instances are localizable to work areas in which etiologic agents may be identified and removed. In addition to malignancies, other chronic disease excesses have been demonstrated by analysis of mortality statistics.

Our investigations also suggest the existence of higher frequencies of some chronic diseases such as dermatitis, which can not be identified through study of death certification, and others such as chronic pulmonary disease, which are more effectively ascertained through appraisals of functional status.

Recognizing that disease manifestations today may reflect exposures of decades ago, and that many of the potential risks of today's occupational exposures may not be expressed in the incidence of frank chronic disease for decades to come, we have initiated research into early warning systems. Biochemical and physiologic indicators measured before the appearance of symptoms or clinical signs, are the ideal. During their research development, we are exploring the feasibility and utility of ongoing surveillance through the use of selected survey questionnaires, and the standardized collection of health and sickness behavior information, including sickness absenteeism, hospitalization and disability retirement. This infor-

mation, combined with standardized work histories and environmental measurements provides the potential for identification of previously unknown occupational causes of chronic disease, and also the monitoring required to ascertain and remove known hazards.

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